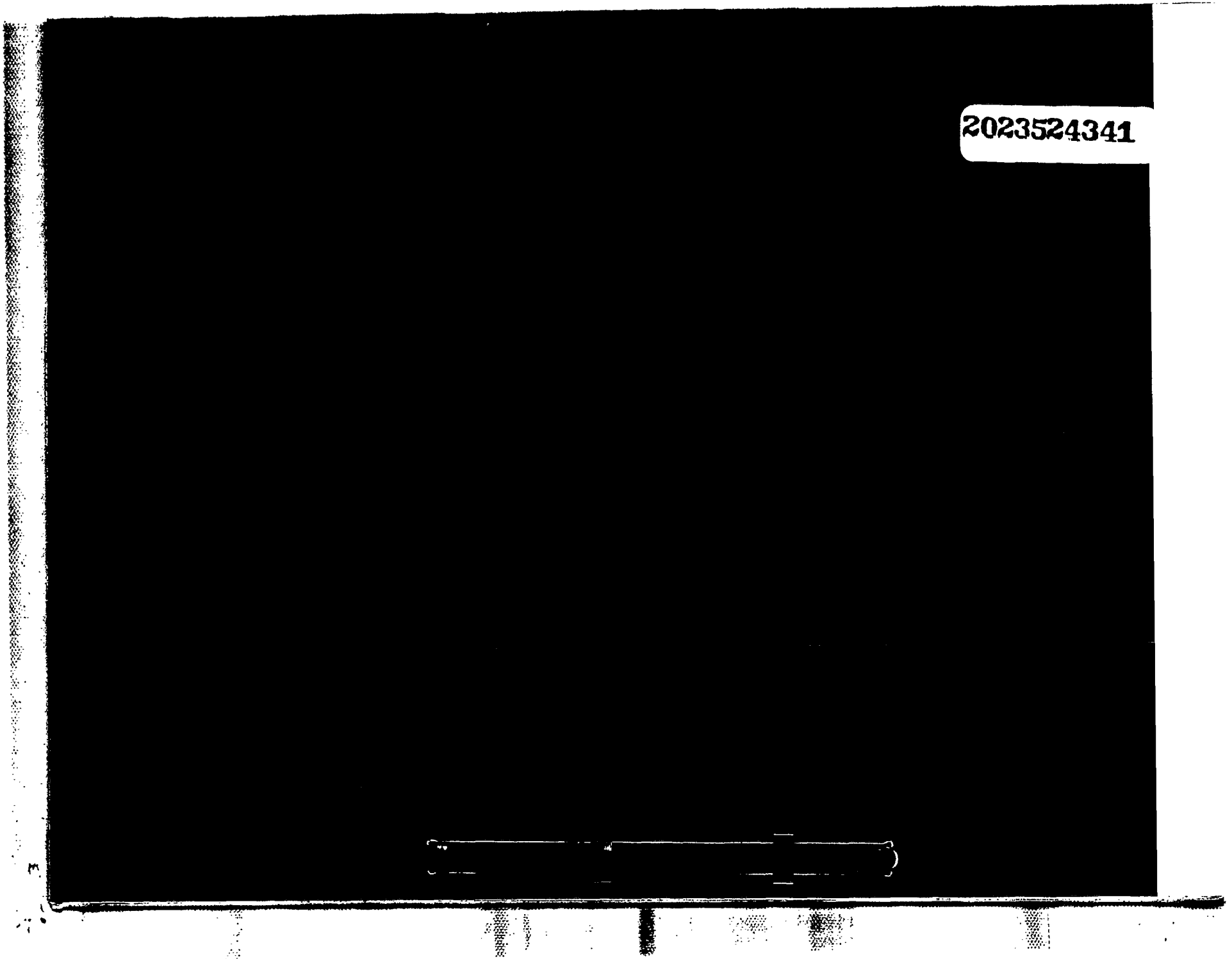

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OAK RIDGE NATIONAL LABORATORY
OPERATED BY MARTIN MARIETTA ENERGY SYSTEMS, INC.

POST OFFICE BOX 2009
OAK RIDGE, TENNESSEE 37831

April 9, 1991

Center for Indoor Air Research
1099 Winterson Road, Suite 280
Linthicum, Maryland 21090
Atten: Dr. Alice Zeiger

Dear Dr. Zeiger:

I am enclosing a draft copy of a proposal entitled "Treatment of overdispersed, aggregated data on human chromosomal aberrations," along with nine copies for possible funding for 1992, 1993, and 1994.

I am submitting it as an informal document because our organization's prime contractor, Department of Energy, does not permit me to submit it formally. If you consider it worth funding and if you are willing to write a letter of acceptance, then our Work for Others Office will proceed with formal proposal. I appreciate your understanding in this matter.

This proposal is a joint effort with Dr. Marvin A. Kastenbaum and he is submitting a proposal separately almost identical to my proposal. My organization, Oak Ridge National Laboratory, requires (by the regulation of the Department of Energy) an overhead charge of 50%. In my proposal, I am asking 50% overhead even though you have stated in your guidelines that the maximum overhead charge is 25%. Is there a possiblity that you will allow the 50% overhead on my proposal since Dr. Kastenbaum will not be charging any overhead cost? Overhead cost is the major reason that we are submitting a proposal separately.

I hope this will meet with your approval. Thank you very much for your consideration.

Sincerely Yours,

K O Bowman

Kimiko O. Bowman
Engineering Physics and
Mathematics Division

KOB:dch

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CENTER FOR INDOOR AIR RESEARCH
1099 WINTERSON ROAD
SUITE 280
LINTHICUM, MD 21090
(301) 684-3777
FAX (301) 684-3729

APPLICATION FOR RESEARCH CONTRACT

1. PRINCIPAL INVESTIGATOR. Name, title, telephone # and mailing address.

(a) Kimiko O. Bowman (Name) (b) Sr. Research Scientist (Title) (c) (615) 574-3126 (Telephone number)

(d) Engineering Physics and Mathematics Division (Department) (e) Oak Ridge National Laboratory (Institution)

(f) P.O. Box 2008, Bldg. 6012, Oak Ridge (Mailing Address) (g) Tennessee 37831-6367 (State/Zip)

2. PROJECT TITLE. (Do not exceed 75 typewriter spaces inclusive of spaces between words and punctuation.)
Treatment of overdispersed, aggregated data on human chromosomal aberrations.

3. KEY WORDS. Please provide three (3) key words which will be used as reference headings.
Aggregated data, Chromosomal aberrations, and Overdispersion.

4. INSTITUTION. Name and address of institution responsible and accountable for disposition of funds awarded on the basis of this application.

(a) Oak Ridge National Laboratory (Institution) (b) P. O. Box 2008, Building 6012 (Street Address)

(c) Oak Ridge (City) (d) Tennessee 37831-6367 (State/Zip)

5. LOCATION. List location where research will be conducted *if other than institution identified in #4 above.*

(a) Fort Myers, Florida, (Co PI, Dr. M. A. Kastenbaum)

(b) University of Georgia, Athens, Georgia (Consultant, Dr. L. R. Shenton)

6. INCLUSIVE DATES and TOTAL COSTS of this specific project related to each 12 month period if more than one year is required to complete project. Summarize from budget page, item 13(j). It must be understood that awards for 2nd and 3rd periods are dependent on Science Advisory Board review and Center approval of continuation application.

	Inclusive Date			Total Cost
(a) 1st 12 month period if required	January 1, 1992	thru	December 31, 1992	$ 69,000
(b) 2nd 12 month period	January 1, 1993	thru	December 31, 1993	$ 68,325
(c) 3rd 12 month period	January 1, 1994	thru	December 31, 1994	$ 72,150

7. INSTITUTIONAL OFFICER. Name, title and telephone # of individual authorized to sign for the institution identified in #4 above. It is understood that the officer, in applying for a contract, has read and found acceptable the Center's Management of Research Contracts and Contract Administration Policy.

(a) A. W. Trivelpiece (Name) (b) Director, Oak Ridge National Labortory (Title)

(c) _____ (Telephone) (d) _____ (Signature of institutional officer) (e) _____ (Date)

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8. AIMS*. Please be specific. SEE Page 7

(a) Hypothesis

(b) Objectives

9. SIGNIFICANCE OF PROPOSED WORK* SEE Page 8

(a) Background

(b) Literature

(c) Identification of gaps in proposed research area

(d) Project importance

10. PRELIMINARY STUDIES* SEE Pages 9-20

(a) Feasibility of proposed research

(b) Qualifications of investigator

11. EXPERIMENTAL PLAN* SEE Pages 9-20

(a) Design

(b) Methods

(c) Analysis of data

(d) Interpretation of results

(e) Timetable for the investigation

(f) Literature cited

12. AVAILABLE FACILITIES AND RESOURCES SEE Page 21

12A. OTHER SUPPORT SEE Page 22

List all currently active and pending support for all key personnel involved in this proposal. Include the source of support, percentage of appointment, dates of project, a brief description of the project and whether it overlaps, duplicates, replaces, or supplements this proposed work in any way.

* Append as much material as required. TYPE, single space, use 8-1/2" x 11" white paper and label each sheet with name of the principal investigator in upper right hand corner and page number at the bottom. Consecutively number each addendum beginning with page 5. Do not insert pages between pages 1 and 6, e.g. 2a, 2b, 3a, etc. Include nine copies and an original. If sending photographs, include 2 original sets.
Note: All nine copies *must* be placed in a press board binder per mailing instructions.

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13. BUDGET. Detail specific needs for first 12-month period. Estimate category sub-totals for 2nd and 3rd periods, if required. Append justifications.

		$ 1st period	$ 2nd period	$ 3rd period
(a) Salaries, List personnel by name and title. Indicate individuals % time to be spent on this project.				
%	Professional:			
	Kimiko O. Bowman, Ph.D., Dr. Engr.		REDACTED	
	Technical:			
	Other:			
	Fringe benefits payable at institution's rate of _____%			
	Category (a) Sub-Total		REDACTED	
(b) Consultants (per diem, travel & expenses):				
	Category (b) Sub-Total	$	$	$
(c) Supplies & Expense: Consumables (by category)				
	Computer Service	6,000	6,500	7,000
	Animals and related costs			
	Other expenses (itemize)			
	Publication	1,000	1,050	1,100
	Category (c) Sub-Total	$ 7,000	$ 7,500	$ 8,100
(d) Travel & Expenses:				
	Working at three locations and attend professional meeting 2 times a year	6,000	6,500	7,000
	Category (d) Sub-Total	$ 6,000	$ 6,500	$ 7,000
(e) Alterations and Renovations				
	Category (e) Sub-Total	$	$	$
(f) Sub-contracts				
	Category (f) Sub-Total	$	$	$

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	Category (g) Sub-Total	$	$	$
(g) Equipment				
Printer		3,000		
(h) TOTAL DIRECT COSTS			REDACTED	
(i) Indirect costs not to exceed 25% of the sum of (a) thru (f):		$ 23,000	$ 22,775	$ 24,050
(j) TOTAL PROJECT COSTS			REDACTED	

14. BIOGRAPHICAL SKETCH of all professional personnel listed in 13(a). Append. Please include the following: Name, title, education, scientific field, major research interest, research and/or professional experience and publications. (Limit list of publications to the 20 most important and/or relevant.)

See 12-15

15. a) Are HUMAN SUBJECTS to be used in this research? _____ Yes ___X___ No

If yes, attach Institutional Review Board approval for procedures involving human subjects.

b) Are LABORATORY ANIMALS to be used in this research? _____ Yes ___X___ No

If yes, attach Institutional Animal Care and Use Committee approval for procedures involving animals.

16. If you wish to recommend peer reviewers (outside of your institution) for this proposal, please append their names, addresses, and telephone numbers. Recommendations of peer reviewers are not an application requirement.

Dr. Richard B. Setlow, Brookhaven National Laboratory

17. SIGNATURE OF PRINCIPAL INVESTIGATOR: It is understood that the applicant in applying for a Contract has read and found acceptable the Statements of Policy and Terms Under Which Project Contracts Are Made appearing in the application package.

Kenneth O Bowman Date 4/9/91

Signature of Principal Investigator

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rev. 5/90

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3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION *(from front side)*

According to 45 CFR 46.121, if an application is made to HHS requiring certification and involving use of an investigational new drug or device, additional information is required. In addition, according to 21 CFR 312.1(a)(2), 30 days must elapse between date of receipt by FDA of Form FD-1571 and use of the drug, unless the 30 day delay period is waived by FDA.

3a. INVESTIGATIONAL NEW DRUG EXEMPTION *(if more than one is involved, list others below under NOTES):*

SPONSOR NAME

DRUG NAME

DATE OF END OF 30-DAY EXPIRATION OR WAIVER	NUMBER ISSUED

3b. INVESTIGATIONAL DEVICE EXEMPTION:

SPONSOR NAME

DEVICE NAME

Unless notified otherwise by FDA, under 21 CFR 812.2(b) (ii) a sponsor is deemed to have an approved IDE if: (1) the IRB has agreed with the sponsor that the device is a nonsignificant risk device; and (2) the IRB has approved the study. *(Check applicable box.)*

☐ The IRB agrees with the sponsor that this device is a nonsignificant risk device.

OR

☐ The IDE application was submitted to FDA on *(date)* _____. Number issued _____.

NOTES:

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OMB No. 0925-0637

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ EXEMPTION (previously undesignated)

☐ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ New ☐ Competing continuation ☐ Noncompeting continuation ☐ Supplemental

APPLICATION IDENTIFICATION NO. *(if known)*

POLICY: A research activity involving human subjects that is not exempt from HHS regulations may not be funded unless an Institutional Review Board (IRB) has reviewed and approved the activity in accordance with Section 474 of the Public Health Service Act as implemented by Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46—as revised). The applicant institution must submit certification of IRB approval to HHS unless the applicant institution has designated a specific exemption under Section 46.101(b) which applies to the proposed research activity. Institutions with an assurance of compliance on file with HHS which covers the proposed activity should submit certification of IRB review and approval with each application. (In exceptional cases, certification may be accepted up to 60 days after the receipt date for which the application is submitted.) In the case of institutions which do not have an assurance of compliance on file with HHS covering the proposed activity, certification of IRB review and approval must be submitted within 30 days of the receipt of a written request from HHS for certification.

1. TITLE OF APPLICATION OR ACTIVITY

2. PRINCIPAL INVESTIGATOR, PROGRAM DIRECTOR, OR FELLOW

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION *(see reverse side)*

4. HHS ASSURANCE STATUS

☐ This institution has an approved assurance of compliance on file with HHS which covers this activity.

_____ Assurance identification number _____ IRB identification number

☐ No assurance of compliance which applies to this activity has been established with HHS, but the applicant institution will provide written assurance of compliance and certification of IRB review and approval in accordance with 45 CFR 46 upon request.

5. CERTIFICATION OF IRB REVIEW OR DECLARATION OF EXEMPTION

☐ This activity has been reviewed and approved by an IRB in accordance with the requirements of 45 CFR 46, including its relevant Subparts. This certification fulfills, when applicable, requirements for certifying FDA status for each investigational new drug or device. *(See reverse side of this form.)*

_____ Date of IRB review and approval. *(If approval is pending, write "pending." Followup certification is required.)*
(month/day/year)

☐ Full Board Review ☐ Expedited Review

☐ This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by 45 CFR 46 will be reviewed and approved before they are initiated and that appropriate further certification *(Form HHS 596)* will be submitted.

☐ Human subjects are involved, but this activity qualifies for exemption under 46.101(b) in accordance with paragraph _____ *(insert paragraph number of exemption in 46.101(b), 1 through 5)*, but the institution did not designate that exemption on the application.

6. Each official signing below certifies that the information provided on this form is correct and that each institution assumes responsibility for assuring required future reviews, approvals, and submissions of certification.

APPLICANT INSTITUTION	COOPERATING INSTITUTION
NAME, ADDRESS, AND TELEPHONE NO.	NAME, ADDRESS, AND TELEPHONE NO.
NAME AND TITLE OF OFFICIAL *(print or type)*	NAME AND TITLE OF OFFICIAL *(print or type)*
SIGNATURE OF OFFICIAL LISTED ABOVE *(and date)*	SIGNATURE OF OFFICIAL LISTED ABOVE *(and date)*

HHS 596 (Rev. 1/82) *(If additional space is needed, please use reverse side under "Notes.")*

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8. AIMS:

This document proposes an extension, for a period of three additional years, of the research carried out by K. O. Bowman and M. A. Kastenbaum with CIAR support on the optimal design of laboratory experiments involving mutagenicity tests of chemical components. Our investigations to date have revealed that the **problem of overdispersion of binomial and Poisson data**, resurrected by us after twenty years of dormancy, is intrinsic to the consideration of **experimental-design optimality involving chromosomal aberrations**. Moreover, the current literature in genetics reveals that this problem is **relevant and important to those geneticists working with large, aggregated data sets.** And our own work has shown that this problem is almost certainly susceptible to solution by new and powerful mathematical and statistical techniques.

The tractability of these formerly intractable methods is due, in great part, to computer technology which has evolved in parallel with the collection and aggregation of large quantities of biological data. Techniques of analysis of such data that are currently in vogue - **meta-analysis, Poisson-regression,** etc. - can no longer rely on the usual simplifying assumptions about underlying distributional properties of the aggregated data. Instead, new distributions that characterize the aggregated data more realistically must be considered and applied. To date, **we have developed a number of such distributions** (6, 7, 8), and we are in the process of developing others. **We will be applying these distributions to large aggregations of data on human chromosomal aberrations** (2, 3, 4, 5). We will also examine the relevancy of our new distributions to **recent developments in Poisson-regression.** Our findings will be **applicable to similar biological endpoints said to result from exposure to environmental tobacco smoke.**

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9. SIGNIFICANCE OF PROPOSED WORK:

The problem of overdispersion of binomial and Poisson data is intrinsic to the consideration of **experimental-design optimality involving human chromosomal aberrations.** Recent literature on chromosomal aberrations reveals that this problem is recognized by geneticists who work with large, aggregated data sets (5). They know that Statistical analyses to determine the significance of differences in chromosomal aberrations between groups, or experimental treatments, are based on the assumption of an underlying Poisson distribution (10, 20) of the data. The validity of such analyses rests on the condition that aberrations in "control cells", (untreated, normal), do indeed follow the Poisson distribution. However, because of the low frequency with which such aberrations arises, this conditions has seldom, if ever, been adequately tested. Now, **with recently aggregated, large data sets (3, 4, 5) such checks on the distributional properties of chromosomal aberrations are practical and feasible.**

In human cytogenetics, the collection of large numbers of cells from many individuals involves the participation of many technicians, working in different laboratories, under varying conditions, for long periods of time. All of these factors tend to contribute additional variation, over and above Poisson, to the aggregated numbers upon which statistical tests are ultimately performed. If the aggregated data are assumed to follow a Poisson distribution, the variances are taken to be equal to the means. This fact becomes important in weighted regression analysis and in hypothesis testing. In weighted regression, the weights are generally taken as the inverse of the variance, which, in the case of Poisson variables is equal to the mean. **If, by virtue of overdispersion, the weights are too large, the resulting analysis will be distorted.**

In the realm of hypothesis testing, the variance, or a function thereof, is featured as the denominator of a ratio, whose numerator is a function of the mean. If additional variation, introduced by the factors mentioned above, is not taken into account, the denominator will be smaller than it should be, and the resulting ratio will be larger. This will result in a test stattistic that rejects the null hypothesis more often than it should. In the parlance of statistics, the Type I error will be increased, and the level of significance will be decreased. For example, if the level of significance is taken as 95%, **researchers will conclude that a "significant difference, ($p < 0.05$)" exists, more often than they should.** It also follows that test statistics that are designed to test for adverse effects of environmental hazards (using dose-response analysis) may overstate the significance of effects if overdispersion in present in the data.

These problems and others are alluded to in recent literature (1, 5) on observed chromosomal aberrations said to be induced by ionizing radiation. In fact, the same problems would arise when other clastogen, are tested for their alleged ability to induce chromosomal aberrations. This concern is especially **relevant to chromosomal aberrations, including sister chromatid exchanges in humans (9, 18, 19, 21, 22), said to be induced by ambient tobacco smoke.**

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10. PRELIMINARY STUDIES and EXPERIMENTAL PLAN:

To date, we have submitted for publication two manuscripts (6, 8), and third (7) is in its final stages of preparation. Copies of these documents have been forwarded to CIAR as reports of progress of our research accomplishments since January 1990.

Our intent now is to establish **close working relationships with other investigators,** whose interests in specific aspects of our project will result in collaborations that are of mutual benefit. In particular, Dr. Kastenbaum will establish a collaborative working relationship with **Dr. Michael A Bender of the Brookhaven National Laboratory.** Dr. Bender possesses and has access to **large data sets on human chromosomal aberrations** said to be induced by exposure to an assortment of chemical and radiological agents. Analyses have been performed on some subsets of these data, and the results have been reported in the literature (3, 4, 5). Much work remains to be done, however, specifically in **clarifying the various causes of overdispersion** associated with some chromosomal aberrations and not with others. Such clarification will make the new and complex distributions, developed by us, **more meaningful to the geneticists.** Dr. Kastenbaum plans to collaborate with Dr. Bender in this undertaking.

Some of the other questions that will be addressed deal with the nature of the aggregated data, proper **approaches to their analysis,** and **philosophically-acceptable foundations for the inferences** drawn from such analyses. Such considerations of these aggregated data will be immediately **relevant and applicable** to similar data collected in the quest for **alleged genetic effects of environmental tobacco smoke.**

At the same time, Dr. Bowman will establish a closer working relationship with **Dr. E. L. Frome,** her colleague at the Oak Ridge National Laboratory. Dr. Frome has published a number of papers on the subject of **Poisson regression** (11, 12, 13, 14, 15, 16), and is an acknowledged expert and leader in this field. The relevance of this collaboration to our proposed project is readily apparent in some of Dr. Frome's publications. His work encompasses the application of Poisson regression techniques to **log-linear, quasilinear, and nonlinear models,** as well as to **epidemiologic follow-up data** organized into a **life-table** type format. **Overdispersed Poisson** distributions would affect such analyses by virtue of expected changes in the covariance matrix.

One specific application of Frome's work (12), is a reanalysis of the Doll-Hill data on lung cancer deaths among British physicians. Of particular interest in Frome's analysis is his finding that the **treatment of data on nonsmokers** is of critical importance to the results of the analysis. Frome demonstrates that estimates of the background death-rate when nonsmoker data are excluded from the analysis, is "seven times lower than the estimate obtained when data for nonsmokers are included". These findings, on the **impact of nonsmoker data** on the results of epidemiological analyses of the alleged effects of tobacco smoke, are directly relevant to **CIAR concerns** with the biological effects on nonsmoking humans that are said to result from **environmental tobacco**

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smoke.

We will also continue to collaborate with **Dr. L. Roy Shenton** (University of Georgia). His interests in practical analyses of statistical models, especially those dealing with estimation problems associated with distributions, has spanned many years, and in collaboration with Dr. Bowman has produced new results using computer oriented approaches.

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CURRICULUM VITAE

Kimiko O. Bowman

MAILING ADDRESS

Oak Ridge National Laboratory
Building 6012, P.O. Box 2008
Oak Ridge, Tennessee 37831-6367

EDUCATION

Dr. Engr. REDACTED

Dissertation title: Small Sample Properties of Statistics - Computer Oriented Algorithmic Approach
Major Professor: Shuni-chi Amari

Ph.D. REDACTED

Dissertation title: Moments to Higher Orders for Maximum Likelihood Estimators with an Application to the Negative Binomial Distribution
Major Professor: L. R. Shenton

M.S. REDACTED

Thesis title: Estimation of the Strength of a Radioactive source
Major Professor: H. A. David

B.S. REDACTED

EMPLOYMENT

8/63-present	ORNL-- Computing Technology Center; Mathematics Division; Computer Sciences Division; Engineering Physics and Mathematics Division
1990-present	University of Tennessee (Professor of Mathematics)
1971-73	University of Tennessee (Assistant Professor, Honorary)
1966-67	University of Tennessee (Instructor, Part-time)
1968	University of Georgia (Visiting Professor)

EXPERIENCE

- Currently Senior Research Scientist in the Mathematical Sciences Section of the Engineering Physics and Mathematics Division. The research is conducted under the Statistical Methods Project, specifically in the topics of distributional properties of estimators and test statistics under non- normal sampling; the methodologies include computational algorithms, summation of divergent series, numerical analysis, etc. The research results have wide application, since non-normal distributions have been used more and more for natural models, for example distribution of stress of reactor vessel is considered as the Weibull distribution, the risk or survival curve is considered as gamma or Weibull, etc.
- Consulting with colleagues on various aspects of statistics within Oak Ridge National Laboratory, Oak Ridge Gaseous Diffusion Plant and Y-12 Plant; for example, procedures for validating computer models in economics and stochastic

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models in epidemiology and biology, find suitable approximations of distribution for Laser stress, etc.

- Extensive experience in statistical computation in the area of developing new algorithms for approximations to distributions, new algorithms to compute higher cumulants and moments, etc., numerical analysis related to asymptotic series developing new theories and algorithms of summing divergent series, and random number generators for massively parallel computers.
- Served as principal thesis advisor for graduate students from the Oak Ridge Associated Universities Fellowship Program and the Mathematics Department of the University of Tennessee.

HONORS AND AWARDS

- Virginia State Scholarship, REDACTED
- Sears Roebuck Scholarship, REDACTED
- Mathematics Department Scholarship,
- Elected member of Kappa Delta Pi, Kappa Mu Epsilon, Chi Beta Phi
- Award: Chi Beta Phi of the Year, REDACTED
- Graduated with Honors in Mathematics from Radford University
- Grant: National Institute of Health Research Fellow, REDACTED
- Fellow: American Association for the Advancement of Science,
- Fellow: American Statistical Association, REDACTED citation stated: "for contributions to the quantities assessment of distributional properties of estimators in small samples: for skill in programming for a wide variety of applied statistical problems, and effective consulting and collaboration with scientists and engineers."
- Ordinary Member: International Statistical Institute, REDACTED
- Fellow: Institute of Mathematical Statistics, R citation stated: for her leadership in combining numerical analysis and computing with statistical theory, contributions to the study of higher order moments of maximum likelihood estimators and small sanple properties of statistics, and for her service in opening the statistical profession to new members.
- Recipient: Outstanding Alumnus R award from Radford University, R
- Recipient: Distinguished and Sustained Contributions to Science Award, AWIS, R
- Recipient: Technical Achievement Award, Martin Marietta Energy Systems, Inc.
- Citation Classics: REDACTED The paper entitled "Tables for determining statistical significance of mutation frequencies" coauthored with M. A. Kastenbaum was designated as *Citation Classics*, R

PROFESSIONAL ACTIVITIES

- Liaison Scientist: Office of Naval Research, Department of Navy, REDACTED
- Panelist: Women in Science Program, National Science Foundation, REDACTED
- Panelist: Visiting Professorship of Women Program, National Science Foundation, REDACTED

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- Panelist: Scientific Computing Research Equipment for the Mathematical Sciences, National Science Foundation, R
- Member: International Editorial Board, Communication in Statistics, REDACTED
- Member: American Statistical Association Committee of Representatives to the American Association for the Advancement of Science, R
- Member: American Association for the Advancement of Science Committee of Section T-Information, Computing and Communication, R
- Member: National Science Foundation Advisory Committee on Equal Opportunities in Science and Engineering, R
- Member: National Science Foundation Task Force on Persons with Disabilties, R
- Chair: Subcommittee on the Persons with Disabilities, National Science Foundation Advisory Committee on Equal Opportunities in Science and Engineering, R
- Associate Editor: Journal of Statistical Computation and Simulation, REDACTED
- Member: Editorial Advisory Board, Journal of Statistical Computation and Simulation, R
- Reviewer for National Science Foundation, grant proposal
- Reviewer for Science, American Association for the Advancement of Science
- Contributing Editor: Current Index to Statistics, R
- Lecturer: Visiting Lecture Program, Committee of Presidents of Statistical Societies (COPSS), R
- Member of advisory panel, AAAS, National Network of Minority Women in Science, R
- Chair: Coordinating Committee on Equal Opportunity in Statistics, American Statistical Association, R
- Member: Advisory Committee, Data Base Study, Educational Testing Center, R
- Invited speaker for numerous international conferences.

MEMBERSHIP

REDACTED REDACTED

PUBLICATIONS (20 selected)

K. O. Bowman

Shenton, L. R. and Bowman, K. O. (1963). "Higher moments of a maximum-likelihood estimator", *J. Roy. Statist. Soc., Ser. B.*, 25, 305-317.

Newell, Guy R., Harris, W. W., Bowman, K. O., Boone, C. W. and Anderson, N. G. (1968). "Evaluation of 'Virus-Like' particles in the plasmas of 255 patients with leukemia and related diseases," *New Eng. J. of Med.*, 278, 1185-1191.

Bowman, K. O., Hutcheson, K., Odum, E. P. and Shenton, L. R. (1971). "Comments on the

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distribution of indices of diversity," *Statist. Ecol., Vol. 3: Many Species Populations, Ecosystems, and Systems Anal.*, ed., G. P. Patil, E. C. Pielow and W. E. Waters, Pennsylvania State University Press, 315-366.

Shenton, L. R. and Bowman, K. O., and Sheehan, D. (1971). "Sampling moments of moments associated with univariate distribution," *JRSS Ser. B*, 33, 444-457.

Bowman K. O. (1972). "Tables of the sample size requirement," *Biometrika*, 59, 234.

Bowman, K. O. (1973). "Power of the kurtosis statistic (b_2) in tests of departures from normality," *Biometrika*, 60, 623-628.

Bowman, K. O. and Shenton, L. R. (1973). "Notes on the distribution of $\sqrt{b_1}$ in Ssmpling from Pearson distributions," *Biometrika*, 60, 155-167.

Bowman, K. O. and Kastenbaum, M. A. (1975). *"Sample size requirement: Single and double classification experiment, Selected Tables in Mathamatical Statistics"*, American Mathematical Society and Institute of Mathematical Statistics, ed., D. B. Owen and H. L. Harter, 111-232.

Bowman, K. O. and Shenton, L. R. (1975). "Omnibus" test contours for departures from normality based on $\sqrt{b_1}$ and b_2, *Biometrika*, 62, 243-250.

Pearson, E. S., D'Agostino, R. B. and Bowman, K. O. (1977). "Test for departure from normality: Comparison of powers," *Biometrika*, 64, 231-246.

Bowman, K. O. and Shenton, L. R. (1977). "Approximate percentage points for Pearson distribution," *Biometrika*, 66, 147-151.

Shenton, L. R. and Bowman, K. O. (1977). *Maximum Likelihood Estimation in Small Samples*, England: Charles Griffin and Co., Ltd.

Bowman, K. O. and Shenton, L. R. (1982). "Approximations to distributions," *Encyclopedia of Statistical Sciences*, Vol. 1, ed., Samuel Kotz and N. L. Johnson, John Wiley and Sons, Inc., 107-118.

Bowman, K. O. and Shenton, L. R. (1983). "Johnson's Translation System," *Encyclopedia of Statistical Sciences*, Vol. 4, ed., Samuel Kotz and N. L. Johnson, John Wiley and Sons, Inc., 303-314.

Bowman, K. O. (1984). "Extended moment series and the parameters of the negative binomial distribution," *Biometrics*, 40, 249-252.

Bowman, K. O., Shenton, L. R., and Bernard, C. R. (1985). "Study of age dependent half-life of Iodine in man: A reinforcement-depletion urn model," *Bull. Math. Biol.*, 47, 205-214.

Bowman, K. O. and Shenton, L. R. (1986). "A reinforcement-depletion urn model: A contiguity case," *Annals of the Institute of Statistical Mathematics*, 38(2), 233-243.

Bowman, K. O. and Shenton, L. R. (1986), "Moment ($\sqrt{b_1}, b_2$) Techniques," *Handbook of Goodness of Fit Techniques*, ed., R.B. D'Agostino and M. Stephens, Marcel Dekker, Inc., 277-327.

Bowman, K. O. and Shenton, L. R. (1988). *Properties of Estimators for the Gamma Distribution*, Marcel Dekker, Inc.

Bowman, K. O. and Shenton, L. R. (1989). *Continued Fractions in Statistical Applications*, Marcel Dekker, Inc.

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CURRICULUM VITAE

Marvin A. Kastenbaum

MAILING ADDRESS:

REDACTED

EDUCATION

Ph.D.	Statistics, North Carolina State University
M.S.	Statistics, North Carolina State University
B.S.	Mathematics, City College of New York

REDACTED

EMPLOYMENT

1970-1987	Director of Statistics The Tobacco Institute, Washington, D.C.
Summer 1969	Visiting Professor Stanford University, Stanford, California
1968-1970 1960-1967 1956-1960	Special Advisor on Statistics Chief–Biometrics Section Biometrician Oak Ridge National Laboratory, Oak Ridge, Tennessee
1965-1966	Visiting Professor Mathematics Research Center, University of Wisconsin, Madison, Wisconsin
Summer 1955	Consultant Institute of Human Biology, Ann Arbor, Michigan
1953-1954	Biostatistician Atomic Bomb Casualty Commission, Hiroshima, Japan
1952	Chief Statistician Business Information Division, Dun and Bradstreet, Inc., New York, New York
Summers 1948, 1950	Student Assistant Statistician U.S. Bureau of Census, Washington, D.C.

MEMBERSHIP IN PROFESSIONAL SOCIETIES:

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K. O. Bowman

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OTHER ACADEMIC AND PROFESSIONAL ACTIVITIES:

- Lecturer, North Carolina College, REDACTED
- Traveling Lectures, Oak Ridge National Laboratory, REDACTED
- Lecturer, University of Tennessee, REDACTED
- Professor Biometrical Sciences, University of Tennessee, REDACTED
- Visiting Lecturer, National Science Foundation, REDACTED
- Radiological Animal Research Advisory Committee, U.S. Public Health Service, REDACTED
- Bureau of Drugs Advisory Committee, Food & Drug Administration, REDACTED
- Advisory Committee on Hazards of Uranium Mining, National Academy of Sciences, Division of Medical Sciences, REDACTED
- Consultant Climatic Impact Committee, National Academy of Sciences, REDACTED
- Ad hoc Panel on Research Needs for Estimating the Biological Hazards of Low Doses of Ionizing Radiation, National Academy of Sciences, REDACTED
- *Communications in Statistics*, Editorial Board, REDACTED
- Award of Citation Classic R "Tables for determining the statistical significance of mutation frequencies," *Current Contents*, 20.

PUBLICATIONS (20 selected)

Marvin A. Kastenbaum

With W. C. Moloney (1955), "Leukemogenic effects of ionizing radiation on atomic bomb survivors in Hiroshima City," *Science* 121(3139).

With S. N. Roy (1956), "On the hypothesis of 'no-interaction' in a multiway contingency table," *Ann. of Math. Statistics* 27(2).

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With L. Sandler (1958), "A note on the frequency distribution of tetrads by rank in drosophila melanogaster," *Genetics* 43(2).

Kastenbaum, M. A. (1958), "Estimation of relative frequencies of four sperm types in drosophila melanogaster," *Biometrics* 14(2).

With D. E. Lamphiear (1959), "Calculation of chi-square to test the no three-factor interaction hypothesis," *Biometrics* 15(1).

Kastenbaum, M. A. (1959), "A confidence interval on the abscissa of the point of intersection of two fitted linear regressions," *Biometrics* 15(2).

Kastenbaum, M. A. (1960), "The separation of molecular compounds by countercurrent dialysis: a stochastic process," *Biometrika* 47(1)(2).

Kastenbaum, M. A. (1960), "A note on the additive partitioning of chi-square in contingency tables," *Biometrics* 16(3).

Kastenbaum, M. A. (1966), "A dialysis system with one absorbing and one semi-reflecting state," *Jour. Applied Probability* 3.

With M. A Bender and J. B. Davidson (1967), "Chromosome analysis," *Use of Computers in Analysis of Experimental Data and the Control of Nuclear Facilities*, U.S. Atomic Energy Commission, Division of Technical Information.

With M. A Bender (1969), "Statistical analysis of the normal human karyotype," *Amer. Jour. of Human Genetics* 21(4).

With M. A Bender and Claudia S. Lever (1969), "The classification of human chromosomes," *Proceedings of the 37th Session of the International Statistical Institute*, London, England.

Kastenbaum, M. A. (1969), "The consulting statistician: who needs him?" *Review*, Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Kastenbaum, M. A. (1970), "A review of contingency tables," *S.* N. Roy Memorial Volume, Chapter 21, University of North Carolina Press.

With K. O. Bowman (1970), "Tables for determining the statistical significance of mutation frequencies," *Mutation Research* 9.

With D. G. Hoel and K. O. Bowman (1970), "Sample size requirements: one-way analysis of variance," *Biometrika* 57(2).

With D. G. Hoel and K. O. Bowman (1970), "Sample size requirements: randomized block designs," *Biometrika* 57(3).

Kastenbaum, M. A. (1974), "Analysis of categorical data: some well-known analogues and some new concepts," *Communications in Statistics* 3(5).

With K. O. Bowman (1974), "Potential pitfalls of portable power," *Technometrics* 16(3).

With K. O. Bowman (1985), "Optimal sample size requirements," *Encyclopedia of Statistical Sciences* 6.

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K. O. Bowman

BIOGRAPHICAL SKETCHES

L. R. Shenton

EDUCATION

D.Sc.	Edinburgh University	REDACTED
Ph.D.	Edinburgh University	
B.Sc.	Victoria University of Manchester: Hons. Mathematics	

REDACTED

EMPLOYMENT

1984-present
Faculty Associate; Advanced Computational Methods Center, University of Georgia.

1978-1984
Emeritus Professor of Statistics, University of Georgia.

1963-1977
Professor of Statistics, University of Georgia.

1964-1965
Research Staff, Mathematics Division, Oak Ridge National Laboratory.

1962-1964
Professor of Statistics, Virginia Polytechnic Institute, Blacksburg, Virginia.

1957-1962
Reader in Mathematics, Manchester College of Technology, Faculty of Technology, Manchester University.

EXPERIENCE

- Senior scientist for a project (Project Theo) of the U.S. Department of agriculture sponsored by the Naval Air Systems Command, Department of the Navy, from December 1965 to July 1975. Assisted in the statistical analysis of warm-cloud, warm-fog, and other meteorological phenomena at the land-sea interface in southeastern Georgia. The thrust of the project was a study of weather modification experiments of mutual interest in the Department of Defense and the Forest Service.
- Co-investigator for sponsored research at the Oak Ridge National Laboratory (Mathematics Division) on the subject of compartmental models and random difference equations. A paper was read on the subject at the Fifth Berkeley symposium on mathematical statistics.
- Research for the Health Physics Division of the Oak Ridge National Laboratory. The study focused on urn models for the decay of radioactive atoms (iodene in particular) in man, and especially estimates of half-life.
- Sponsored work at the Oak Ridge National Laboratory (Mathematics and Statistics Division) involving:
  a. a computer algorithm for the fast evaluation of maximum likelihood estimators for the parameters of the 2-parameter gamma density, and
  b. a computer algorithm for the evaluation of derivatives of a function of a function in several variables.

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DISSERTATIONS SUPERVISED:

1. Dr. Ray Meyers
   "Orthogonal Statistics"
2. Dr. Kimiko Bowman
   "Higher Moments of a Maximum Likelihood Estimate"
3. Dr. D. Sheehan
   "The Computational Approach to Sampling Moments - A Study of Certain Estimators for the Negative Binomial Distribution"
4. Dr. Kermit Hutcheson
   "The Moments and Distribution for an Estimate of the Shannon Information Measure"
5. Dr. Y. C. Patel
   "Some Problems in Estimation for the Parameters of the Hermite Distribution"
6. Dr. Robert Clifton Bailey
   "A Montage of Diversity"
7. Dr. Thomas Joseph Mason
   "A Statistical Model for Induced Disease"
8. Dr. Robert H. Byers, Jr.
   "Some Approximations to Probability Distributions Using Moments"
9. Dr. Hing-kam Lam
   "The Distribution of the Standard Deviation an Student's t from Non-Normal Universes"
10. Anis Ismail Kanjo
    "The Theory and Application of Transformations in Statistics"
11. Patrick M. Skees
    "Statistical Aspects of Rainfall with Respect to Storms and Weather Modification Experiments"

(1-9 at the Ph.D level; 10-11 at the M.S. level)

PROFESSIONAL AFFILIATIONS

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12. AVAILABLE FACILITIES AND RESOURCES

The Oak Ridge National Laboratory is a multi-purpose research institution, including environmental sciences and biology, in particular, the Mathematical Sciences Section of the Engineering Physics and Mathematics Division has about 35 research personnel with diversified expertize.

In support of its computational and research needs, the investigators have access to a variety of computers at Oak Ridge National Laboratory. The Mathematical Sciences Section operates a Research Computing Facility consisting of a VAX 11/785 with Floating Point Accelerator, an Intel iPSC/860, with 128 processors, 1 gigabytes memory and 5 gigabytes concurrent file storage, a Cogent XTN with 18 transputer, processors, 3 Sun fileservers supporting over 30 workstations. Seven IBM RS6000/530's and four IBM RS6000/320's, a stardent P3000 high-performance graphics workstation, an Intel iPSC/2, and a Sequent Balance 8000. The iPSC/2 computer is a hypercube parallel computer having 64 asynchronous processors and 32 megabytes of memory. The Sequent computer is a bus-based parallel computer with 12 asynchronous processors sharing 16 megabytes of memory. It augments the VAX by providing additional production CPU cycles for the expanding computational and communication needs of the section and provides a computer for testing parallel algorithms for a shared-memory environment. Easily accessible at the Oak Ridge facilities are a Cray X-MP, two IBM 3090s, two VAX 8600s, and other computational equipment typically associated with a large national laboratory. Network access is available to various other computers, such as the Cray 2 at the National Magnetic Fusion Energy Computer Center, Lawrence Livermore National Laboratory and the Cray YMP/4 at the Supercomputer Computations Research Institute, Florida State University.

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12A. OTHER SUPPORT:

1. K. O. Bowman
   - CIAR, 1990-1991, 25%, "Testing the Mutagenicity of Components of Indoor Ambient Air (Co-PI, M. A. Kastenbaum)
   - NSF, 1991, 10%, "Planning Proposal for Supercomputer Applications in Statistics. This grant encourage the PI to submit a formal research grant jointly with computational biologist on an application of statistical theory. New initiated research will enhance CIAR funded research.

2. M. A. Kastenbaum
   - CIAR, 1990-1991, 25%, "Testing the Mutagenicity of Components of Indoor Ambient Air (Co-PI, K. O. Bowman)

3. L. R. Shenton (Consultant)
   - CIAR, 1990-1991, R , "Testing the Mutagenicity of Components of Indoor Ambient Air.

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K. O. Bowman

RESEARCH ABSTRACT

Title of Project: **TREATMENT OF OVERDISPERSED, AGGREGATED DATA ON HUMAN CHROMOSOMAL ABERRATIONS**

Investigators: K. O. Bowman and M. A. Kastenbaum

Institution: Oak Ridge National Laboratory

ABSTRACT:

Our investigations to date have revealed that the problem of overdispersion of binomial and Poisson data is intrinsic to the consideration of **experimental-design optimality involving chromosomal aberrations** alleged to be induced by chemical components in the ambient air. Moreover, the current literature on chromosomal aberrations indicates that the existence of this problem is recognized by geneticists working with large, aggregated data sets. Our research has shown that this problem is almost certainly susceptible to solution by new and powerful mathematical and statistical techniques. Current methods of analysis - meta-analysis, Poisson-regression, etc. - rely on untested, simplifying assumptions about the underlying distributional properties that may not portray the aggregated data accurately. We have developed new, more realistic characterizations (distribution types) that we propose to apply to large aggregations of data on human chromosomal aberrations. Whatever our findings, they will be **applicable to similar biological endpoints said to result from exposure to environmental tobacco smoke.**

Kimberly O Bowman 4/9/91

Signature, Principal Investigator Date

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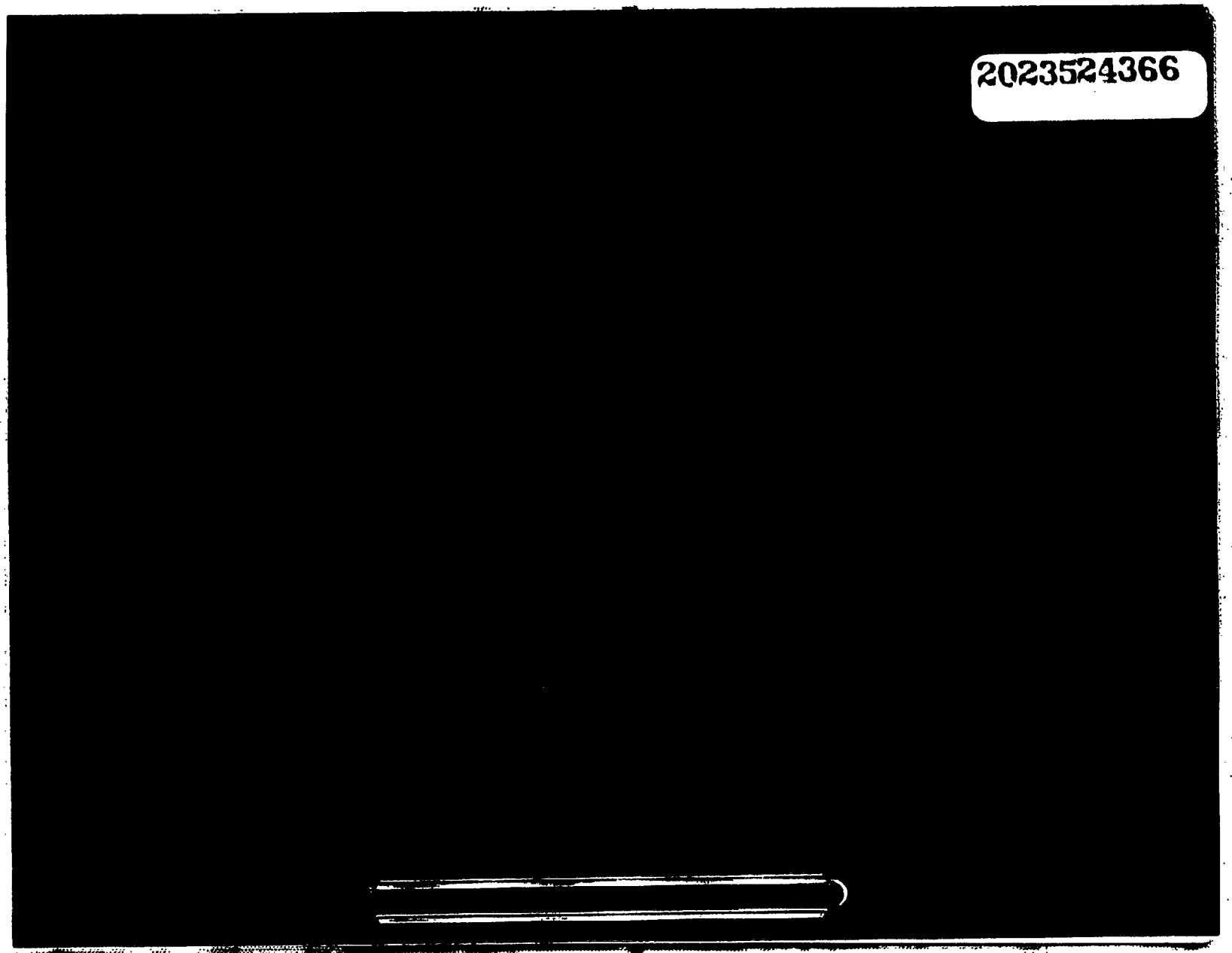

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